

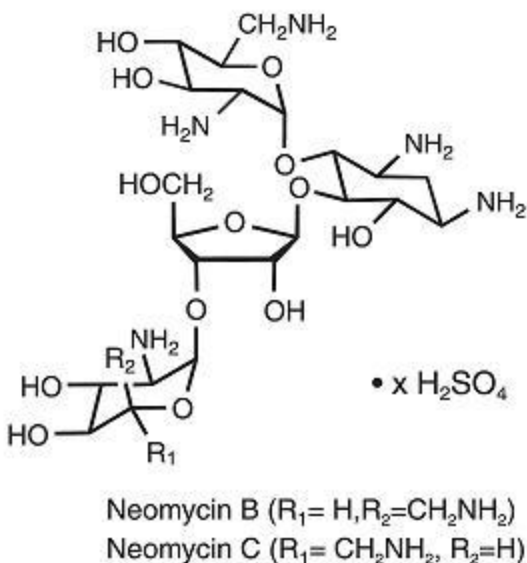
NEOMYCIN AND POLYMYXIN B SULFATES - neomycin sulfate and polymyxin b sulfate solution
X-GEN Pharmaceuticals, Inc.

NOT FOR INJECTION

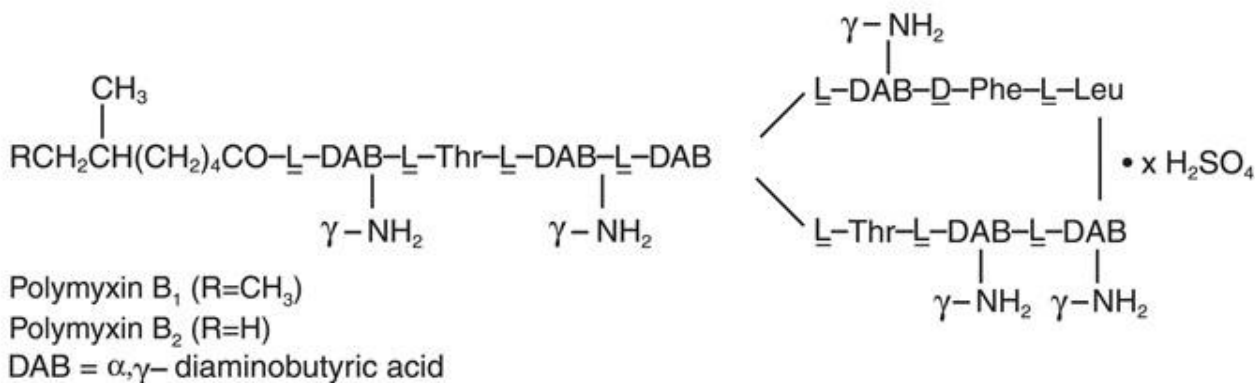
DESCRIPTION

Neomycin and Polymyxin B Sulfates Solution for Irrigation is a concentrated sterile antibiotic solution to be diluted for urinary bladder irrigation. Each mL contains neomycin sulfate equivalent to 40 mg neomycin base, 200,000 units polymyxin B sulfate, and Water for Injection, inactive ingredient: sulfuric acid. The 20-mL multiple dose vial contains, in addition to the above, 1 mg methylparaben (0.1%) added as a preservative.

Neomycin sulfate, an antibiotic of the aminoglycoside group, is the sulfate salt of neomycin B and C produced by *Streptomyces fradiae*. It has a potency equivalent to not less than 600 mcg of neomycin per mg. The structural formulae are:



Polymyxin B sulfate, a polypeptide antibiotic, is the sulfate salt of polymyxin B₁ and B₂ produced by the growth of *Bacillus polymyxa*. It has a potency of not less than 6,000 polymyxin B units per mg. The structural formulae are:



CLINICAL PHARMACOLOGY

After prophylactic irrigation of the intact urinary bladder, neomycin and polymyxin B are absorbed in clinically insignificant quantities. A neomycin serum level of 0.1 mcg/mL was observed in three of 33 patients receiving the rinse solution. This level is well below that which has been associated with neomycin-induced toxicity.

When used topically, polymyxin B sulfate and neomycin are rarely irritating.

Microbiology: The prepared Neomycin and Polymyxin B Sulfates Solution for Irrigation is bactericidal.

The aminoglycosides act by inhibiting normal protein synthesis in susceptible microorganisms. Polymyxins increase the permeability of bacterial cell wall membranes. The solution is active *in vitro* against:

Escherichia coli
Staphylococcus aureus
Haemophilus influenzae
Klebsiella and *Enterobacter* species
Neisseria species, and
Pseudomonas aeruginosa.

It is not active *in vitro* against *Serratia marcescens* and streptococci.

Bacterial resistance may develop following the use of the antibiotics in the catheter-rinse solution.

INDICATIONS AND USAGE

Neomycin and Polymyxin B Sulfates Solution for Irrigation is indicated for short-term use (up to 10 days) as a continuous irrigant or rinse in the urinary bladder of abacteriuric patients to help prevent bacteriuria and gram-negative rod septicemia associated with the use of indwelling catheters.

Since organisms gain entrance to the bladder by way of, through, and around the catheter, significant bacteriuria is induced by bacterial multiplication in the bladder urine, in the mucoid film often present between catheter and urethra, and in other sites. Urinary tract infection may result from the repeated presence in the urine of large numbers of pathogenic bacteria. The use of closed systems with indwelling catheters has been shown to reduce the risk of infection. A three-way closed catheter system with constant neomycin-polymyxin B bladder rinse is indicated to prevent the development of infection while using indwelling catheters.

If uropathogens are isolated, they should be identified and tested for susceptibility so that appropriate antimicrobial therapy for systemic use can be initiated.

CONTRAINDICATIONS

Hypersensitivity to neomycin, the polymyxins, or any ingredient in the solution is a contraindication to its use. A history of hypersensitivity or serious toxic reaction to an aminoglycoside may also contraindicate the use of any other aminoglycoside because of the known cross-sensitivity of patients to drugs of this class.

WARNINGS

PROPHYLACTIC BLADDER CARE WITH NEOMYCIN AND POLYMYXIN B SULFATES SOLUTION FOR IRRIGATION SHOULD NOT BE GIVEN WHERE THERE IS A POSSIBILITY OF SYSTEMIC ABSORPTION. NEOMYCIN AND POLYMYXIN B SULFATES SOLUTION SHOULD NOT BE USED FOR IRRIGATION OTHER THAN FOR THE URINARY BLADDER. Systemic absorption after topical application of neomycin to open wounds, burns, and granulating surfaces is significant and serum concentrations comparable to and often higher than those attained following oral and parenteral therapy have been reported. Absorption of neomycin from the denuded bladder surface has been reported.

However, the likelihood of toxicity following topical irrigation of the intact urinary bladder with Neomycin and Polymyxin B Sulfates Solution for Irrigation is low since no appreciable amounts of these antibiotics enter the systemic circulation by this route if irrigation does not exceed 10 days.

Neomycin and Polymyxin B Sulfates Solution for Irrigation is intended for continuous prophylactic irrigation of the lumen of the intact urinary bladder of patients with indwelling catheters. Patients should be under constant supervision by a physician. Irrigation should be avoided in patients with defects in the bladder mucosa or bladder wall, such as vesical rupture, or in association with operative procedures on the bladder wall, because of the risk of toxicity due to systemic absorption following diffusion into absorptive tissues and spaces. When absorbed, neomycin and polymyxin B are nephrotoxic antibiotics, and the nephrotoxic potentials are additive. In addition, both antibiotics, when absorbed, are neurotoxins: neomycin can destroy fibers of the acoustic nerve causing permanent bilateral deafness; neomycin and polymyxin B are additive in their neuromuscular blocking effects, not only in terms of potency and duration, but also in terms of characteristics of the blocks produced.

Aminoglycosides, when absorbed, can cause fetal harm when administered to a pregnant woman. Aminoglycoside antibiotics cross the placenta and there have been several reports of total, irreversible, bilateral, congenital deafness in children whose mothers received streptomycin during pregnancy. Although serious side effects have not been reported in the treatment of pregnant women with other aminoglycosides, the potential for harm exists. If Neomycin and Polymyxin B Sulfates Solution for Irrigation is used during pregnancy, the patient should be apprised of the potential hazard to the fetus (see PRECAUTIONS).

PRECAUTIONS

General

Ototoxicity, nephrotoxicity, and neuromuscular blockade may occur if Neomycin and Polymyxin B Sulfates Solution for Irrigation ingredients are systemically absorbed (see WARNINGS). Absorption of neomycin from the denuded bladder surface has been

reported. Patients with impaired renal function, infants, dehydrated patients, elderly patients, and patients receiving high doses of prolonged treatment are especially at risk for the development of toxicity. Irrigation of the bladder with Neomycin and Polymyxin B Sulfates Solution for Irrigation may result in overgrowth of nonsusceptible organisms, including fungi. Appropriate measures should be taken if this occurs. The safety and effectiveness of the preparation for use in the care of patients with recent lower urinary tract surgery have not been established. Urine specimens should be collected during prophylactic bladder care for urinalysis, culture, and susceptibility testing. Positive cultures suggest the presence of organisms which are resistant to the bladder rinse antibiotics.

Pregnancy

Teratogenic Effects

Pregnancy Category D. See WARNINGS section.

Pediatric Use

Safety and effectiveness in pediatric patients have not been established.

ADVERSE REACTIONS

Neomycin occasionally causes skin sensitization when applied topically; however, topical application to mucus membranes rarely results in local or systemic hypersensitivity reactions.

Irritation of the urinary bladder mucosa has been reported.

Signs of ototoxicity and nephrotoxicity have been reported following parenteral use of drugs and following the oral and topical use of neomycin (see WARNINGS).

DOSAGE AND ADMINISTRATION

This preparation is specifically designed for use with “three-way” catheters or with other catheter systems permitting **continuous** irrigation of the urinary bladder. The usual irrigation dose is one 1-mL ampul a day for up to 10 days.

Using strict aseptic techniques, the contents of one 1-mL ampul of Neomycin and Polymyxin B Sulfates Solution for Irrigation should be added to a 1,000-mL container of isotonic saline solution. This container should then be connected to the inflow lumen of the “three-way” catheter which has been inserted with full aseptic precautions; use of a sterile lubricant is recommended during insertion of the catheter. The outflow lumen should be connected, via a sterile disposable plastic tube, to a disposable plastic collection bag. Stringent procedures, such as taping the inflow and outflow junction at the catheter, should be observed when necessary to insure the junctional integrity of the system.

For most patients, the inflow rate of the 1,000-mL saline solution of neomycin and polymyxin B should be adjusted to a slow drip to deliver about 1,000-mL every 24 hours. If the patient’s urine output exceeds 2 liters per day, it is recommended that the inflow rate be adjusted to deliver 2,000 mL of the solution in a 24-hour period.

It is important that the rinse of the bladder be **continuous**; the inflow or rinse solution should not be interrupted for more than a few minutes.

Preparation of the irrigation solution should be performed with strict aseptic techniques. The prepared solution should be stored at 4°C, and should be used within 48 hours following preparation to reduce the risk of contamination with resistant microorganisms.

HOW SUPPLIED

Neomycin and Polymyxin B Sulfates Solution for Irrigation are supplied as 1 mL ampul (NDC 39822-1201-1) in boxes of 10 (NDC 39822-1201-2), 50 (NDC 39822-1201-5) and 20 mL Multiple Dose Vial in single Vial cartons (NDC 39822-1220-1).

Storage: Store at 2° to 8°C (36° to 46°F).

Manufactured for:

X-Gen Pharmaceuticals, Inc.

Northport, NY 11768

February 2006

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PACKAGE LABEL.PRINCIPAL DISPLAY PANEL

NDC 39822-1201-1

Neomycin and Polymyxin B Sulfates Solution for Irrigation, USP

STERILE

1 mL

X-GEN PHARMACEUTICALS INC.

FOR IRRIGATION USE ONLY

NOT FOR INJECTION



NDC 39822-1220-2
 Neomycin and Polymyxin B Sulfates Solution for Irrigation, USP
 STERILE
 10 Ampul Carton
 X-GEN PHARMACEUTICALS INC.
 FOR IRRIGATION USE ONLY
 NOT FOR INJECTION



NDC 39822-1220-5
 Neomycin and Polymyxin B Sulfates Solution for Irrigation, USP
 STERILE
 50 Ampul Carton
 X-GEN PHARMACEUTICALS INC.
 FOR IRRIGATION USE ONLY
 NOT FOR INJECTION



NDC 39822-1220-1
Neomycin and Polymyxin B Sulfates Solution for Irrigation, USP
STERILE
20 mL
X-GEN PHARMACEUTICALS INC.
FOR IRRIGATION USE ONLY
NOT FOR INJECTION



NDC 39822-1220-1
Neomycin and Polymyxin B Sulfates Solution for Irrigation, USP
STERILE
Single Vial Carton
X-GEN PHARMACEUTICALS INC.
FOR IRRIGATION USE ONLY
NOT FOR INJECTION

NDC 39822-1220-1

20 mL Multiple Dose Vial

39822-1220-1

Manufactured for:

 Northport, NY 11768

Neomycin and Polymyxin B Sulfates Solution for Irrigation, USP (STERILE)

A concentrated sterile antibiotic solution to be diluted for urinary bladder irrigation.

**FOR IRRIGATION USE ONLY
NOT FOR INJECTION**

PROTECT FROM LIGHT.
RETAIN IN CARTON UNTIL TIME OF USE.


 Rx only

NDC 39822-1220-1

20 mL Multiple Dose Vial

Each mL contains:
 neomycin sulfate equivalent to 40 mg neomycin base;
 200,000 units polymyxin B sulfate; 1mg methylparaben (0.1%) added as a preservative, sulfuric acid and Water for Injection.

Usual Dosage:
 See enclosed package insert.

REFRIGERATE
 Store at 2° to 8°C (36° to 46°F).

PROTECT FROM LIGHT.
RETAIN IN CARTON UNTIL TIME OF USE.


 Rx only

NDC 39822-1220-1

20 mL Multiple Dose Vial

Neomycin and Polymyxin B Sulfates Solution for Irrigation, USP (STERILE)

A concentrated sterile antibiotic solution to be diluted for urinary bladder irrigation.

**FOR IRRIGATION USE ONLY
NOT FOR INJECTION**

PROTECT FROM LIGHT.
RETAIN IN CARTON UNTIL TIME OF USE.


 Rx only

LOT: _____

EXP: _____